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News Release

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FDA Approves MAVENCLAD® (Cladribine) Tablets as First and Only Short-Course Oral Treatment for Relapsing-Remitting and Active Secondary Progressive Multiple Sclerosis

- **MAVENCLAD is the first oral MS treatment to provide two years of proven efficacy with a maximum of 20 days of treatment**
- **MAVENCLAD's unique mechanism may provide an important new option for patients with ongoing active disease**
- **MAVENCLAD demonstrated significant efficacy across key measures of disease activity**
- **Approval is based on clinical program consisting of more than 9,500 patient years of cladribine data and up to 8 years of time on study**

Darmstadt, Germany, March 29, 2019 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced that the U.S. Food and Drug Administration (FDA) has approved MAVENCLAD® (cladribine) tablets for the treatment of adults with relapsing-remitting disease (RRMS) and active secondary progressive disease (SPMS). MAVENCLAD is the first and only FDA approved treatment for RRMS and active SPMS that provides two years of proven efficacy with a maximum of 20 days of oral treatment, during a two-year period.

Because of its safety profile, use of MAVENCLAD is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of multiple sclerosis, and MAVENCLAD is not recommended for use in patients for Clinically Isolated Syndrome (CIS). The MAVENCLAD label includes a boxed warning for potential risk of malignancy, and

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the risk of teratogenicity. The label appropriately defines the relevant associated contraindications.

“Multiple sclerosis is the leading cause of non-traumatic disability in young and middle-aged adults,” said Belén Garijo, CEO Healthcare and Member of the Executive Board of Merck KGaA, Darmstadt, Germany. “We feel privileged to introduce MAVENCLAD into clinical practice in the United States. MAVENCLAD opens a new way to treat MS—a treatment that requires a maximum of 20 days of oral therapy to deliver two years of efficacy to a patient. This approval is a testimony to our long-standing commitment to people living with MS.”

“As an investigator in the clinical trial program, I am pleased MAVENCLAD will now be available to patients in the US. With short treatment courses with pills taken for no more than 10 days in a year and no injections or infusions, MAVENCLAD is an efficacious new treatment option for MS,” said Thomas Leist, M.D., PhD, Director, Comprehensive Multiple Sclerosis Center at Jefferson University Hospitals, Philadelphia, USA. “Nearly 1 million individuals are afflicted with MS in the US alone according to a recent National MS Society sponsored study. MAVENCLAD is a welcome new oral treatment option for this heterogenous and often unpredictable disease.”

Eighty-five percent of people living with MS are initially diagnosed with RRMS, characterized by attacks of new or increasing neurological symptoms. Most people with RRMS will eventually transition to a secondary progressive course in which there is a progressive worsening of neurologic function over time.[1] SPMS can be further characterized at different points as either active (with relapses and/or evidence of new MRI activity) or not active.

“The FDA approval of MAVENCLAD is excellent news for people living with RRMS and active SPMS. MAVENCLAD offers a new and effective option for some of those patients with an oral dosing schedule unlike any other treatment currently available,” said June Halper, CEO of the Consortium of MS Centers. “People living with MS should have the ability to work with their clinician to choose a treatment with a dosing schedule that supports their lifestyle. CMSC congratulates Merck

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KGaA, Darmstadt, Germany, for their dedication to bring MAVENCLAD to the US as the first short-course oral treatment option for the community."

In the clinical trial program, 1,976 patients received therapy for a total of 9,509 patient years, of which the mean time on study including follow-up was approximately 4.8 years and 24% of the follow-up was for eight years. MAVENCLAD demonstrated clinical efficacy across key measures of disease activity, such as annualized relapse rate, disability progression, and magnetic resonance imaging (MRI) activity:

- Patients experienced a 58% relative reduction in the annualized relapse rate with MAVENCLAD compared to placebo (0.14 vs 0.33, $p<0.001$).
- 81% of patients were free of relapses after two years of short-course oral treatment with MAVENCLAD, compared to 63% of patients who received placebo ($p<0.05$).
- Patients treated with MAVENCLAD had a 33% reduction in risk of 3-month confirmed disability progression as measured by Expanded Disability Status Scale (EDSS) compared to placebo ($p<0.05$).
- Patients taking MAVENCLAD experienced a lower median number of T1-weighted gadolinium-enhanced brain lesions and new or enlarging T2 brain lesions compared to patients with placebo (0 vs 0.33 and 0 vs 0.67) $p<0.001$).

The most common (> 20%) adverse reactions reported in the pivotal phase III study, CLARITY were upper respiratory tract infection, headache, and lymphopenia. Serious adverse reactions reported in the clinical program included malignancies (0.27 events per 100 patient-years) in MAVENCLAD treatment arms, compared to placebo patients (0.13 events per 100 patient-years), and herpes zoster infections (2.0% vs. 0.2%) and oral herpes (2.6% vs. 1.2%).

Following the administration of two treatment courses, additional courses of MAVENCLAD are not to be administered. Re-treatment with MAVENCLAD during years three and four may further increase the risk of malignancy. The safety and efficacy of reinitiating MAVENCLAD more than two years after completing two treatment courses has not been studied.

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Merck KGaA, Darmstadt, Germany, is committed to helping support patients prescribed MAVENCLAD. Over the course of 16 years, the company`s comprehensive patient support program in the U.S., MS LifeLines®, has had over four million touchpoints with patients, care partners, health care professionals, and other stakeholders to support our goal of providing one-on-one assistance to U.S. patients prescribed a Merck KGaA, Darmstadt, Germany, MS therapy. MS LifeLines® is now expanding to help patients prescribed MAVENCLAD and offers personalized patient support, including assistance with navigating insurance questions and additional resources that may be able to assist patients who are uninsured or underinsured.

The U.S. approval of MAVENCLAD follows its approval in over 50 countries, including the European Union in August 2017.

For more information on MAVENCLAD, and prescribing information including the boxed WARNINGS, visit www.MAVENCLAD.com.

1. National MS Society. Secondary progressive MS (SPMS). https://www.nationalmssociety.org/What-is-MS/Types-of-MS/Secondary-progressive-MS. Accessed March 2019.

About MAVENCLAD® (cladribine) Tablets (10 mg)
MAVENCLAD, approved by the U.S. Food and Drug Administration (FDA) on March 29th, 2019, is the first short-course oral therapy for the treatment of relapsing forms of multiple sclerosis (RMS). MAVENCLAD is not recommended for use in patients with clinically isolated syndrome (CIS) because of the risk of malignancy. Patients should follow healthcare provider instructions including cancer screening, contraception, and blood tests. The approved dose of MAVENCLAD is 3.5 mg per kg body weight over two years, administered as one treatment course of 1.75 mg per kg per year, each consisting of two treatment weeks. The mechanism by which cladribine exerts its therapeutic effects in patients with multiple sclerosis has not been fully elucidated but is thought to involve cytotoxic effects on B and T lymphocytes through impairment of DNA synthesis, resulting in depletion of lymphocytes. MAVENCLAD causes a dose dependent reduction in lymphocyte counts followed by recovery.

Because cladribine is cytotoxic, special handling and disposal instructions should be followed.

MAVENCLAD has been approved in over 50 countries, including the European Union (EU), Canada, Australia and Switzerland, for various relapsing MS indications.
Visit www.MAVENCLAD.com for more information.

About Multiple Sclerosis
Multiple sclerosis (MS) is a chronic, inflammatory condition of the central nervous system and is the most common, non-traumatic, disabling neurological disease in young adults. It is estimated that approximately 2.3 million people have MS worldwide. While symptoms can vary, the most common

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symptoms of MS include blurred vision, numbness or tingling in the limbs and problems with strength and coordination. The relapsing forms of MS are the most common.

Merck KGaA, Darmstadt, Germany, and Multiple Sclerosis
For more than 20 years, Merck KGaA, Darmstadt, Germany, has been relentlessly focused on understanding the journey people living with MS face in order to create a meaningful, positive experience for them and the broader MS community. However, there is still much that is unknown about this complex and unpredictable disease. Merck KGaA, Darmstadt, Germany, is digging deeper to advance the science and reconstruct a new understanding of MS, inside and out. We are committed to delivering solutions that improve the lives of all those affected by MS.

About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 52,000 employees work to further develop technologies that improve and enhance life – from biopharmaceutical therapies to treat cancer or multiple sclerosis, cutting-edge systems for scientific research and production, to liquid crystals for smartphones and LCD televisions. In 2018, Merck KGaA, Darmstadt, Germany, generated sales of € 14.8 billion in 66 countries.

Scientific exploration and responsible entrepreneurship have been key to the company's technological and scientific advances. This is how Merck KGaA, Darmstadt, Germany has thrived since its founding in 1668. The founding family remains the majority owner of the publicly listed company. Merck KGaA, Darmstadt, Germany holds the global rights to the Merck name and brand. The only exceptions are the United States and Canada, where the business sectors of Merck KGaA, Darmstadt, Germany operate as EMD Serono in healthcare, MilliporeSigma in life science, and EMD Performance Materials.